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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
08/955,570	10/28/97	GREGORY	R 16930-000921

HM12/0413

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EXAMINER	
GUZO, D	
ART UNIT	PAPER NUMBER
1636	8

DATE MAILED: 04/13/99

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on 1/25/99.

☑ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire Three (3) month(s), ~~or thirty days,~~ whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 16-24, 26-41 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☑ Claim(s) 16-24 and 26-41 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☑ Notice of Reference Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

-- SEE OFFICE ACTION ON THE FOLLOWING PAGES --

• U.S. GPO: 1998-409-290/40029

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 16-24, 26-31, 33, 35, 38 and 40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

This rejection is maintained for reasons of record in the previous Office Action (Paper #4) and for reasons outlined below.

Applicants traverse this rejection by asserting that the instant specification provides sufficient guidance on the generation of the claimed vectors, methods of administration of said vectors to humans and animals, appropriate dosages, etc. Applicants assert that each step in the process for carrying out the claimed invention involves methods that are routinely practiced by those of skill in the art and that making of the claimed vectors and administering them to mammals does not require undue experimentation..

Applicants arguments filed 1/25/99 have been carefully considered but are not deemed to be persuasive. It is noted that the claimed invention is not a method of making the claimed

adenoviral vectors or administering said vectors to mammalian subjects, but instead involves adenoviral based gene therapy methods of treating pathologies (such as various cancers) in mammals. It is for the invention as claimed that enablement must exist. Clearly, given the extreme unpredictability and poorly developed state of the viral vector gene therapy art and the absence of teachings in the instant specification whereby the skilled artisan could address and overcome the art recognized hurdles to practicing gene therapy, it must be considered that the skilled artisan would have to have conducted undue and excessive experimentation to practice the claimed invention.

Most of applicants' arguments are directed against a 35 USC 101 (utility) rejection. However, no 35 USC 101 rejection is of record in the prosecution of this application and applicants' arguments are therefore directed to a non-existent rejection. Indeed, the asserted utility of the claimed invention has never been in question. Since no 35 USC 101 rejection is of record, applicants' arguments are not germane to the issues at hand in the prosecution of this application and said arguments will not be addressed further.

To the extent that applicants' remaining arguments pertain to the outstanding 35 USC 112, 1st paragraph rejection of the claims, said arguments will be addressed. Applicants appear to be arguing that gene therapy protocols using viral (i.e. adenoviral) vectors or other delivery vehicles are not sufficiently unpredictable for patentability because numerous clinical trials, involving gene therapy, have been commenced. In response, the examiner notes a more recent article (Nature,

Vol. 392, April 30, 1998, pp. 25-30) by one of the founders of gene therapy, W. French Anderson, wherein Dr. Anderson concludes that:

"Except for anecdotal reports of individual patients being helped, there is still no conclusive evidence that a gene-therapy protocol has been successful in the treatment of a human disease." (Anderson, p. 25). and that "Several major deficiencies still exist including poor delivery systems, both viral and non-viral, and poor gene expression after genes are delivered. The reason for the low efficiency of gene transfer and expression in human patients is that we still lack a basic understanding of how vectors should be constructed, what regulatory sequences are appropriate for which cell types, how *in vivo* immune defenses can be overcome, and how to manufacture efficiently the vectors that we do make." (Anderson, p. 30.).

Applicants, in the instant specification do not specifically address the art recognized hurdles to successful practicing of gene therapy. It is clear, given the cited art concerning gene therapy and the dearth of teachings of the instant specification, that the skilled artisan would need to conduct undue experimentation in order to practice the invention as claimed. Indeed, the broadest claims read on treating any pathology in mammals and it must be considered that the skilled artisan would have to practice trial and error experimentation in order to design a vector with the appropriate transcriptional regulatory sequences for the specific target cells to be treated, overcome immune responses to the vectors, etc.

Applicants indicate that the instant specification provides an *in vivo* example using nude mice into which H69 tumor cells had been introduced and that H69 cells are accepted for use in screening of cancer treatments by the National Cancer Institute.

In response, the examiner notes that the document from SRI International which was provided

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by applicants states that the H69 cells are used for *in vitro* screening of potential anti-cancer drugs and the document provides no evidence that H69 cells introduced into nude mice represents an art recognized model which would be reasonably predictive of results which could be obtained in humans. It is noted that use of animal models for human cancers which utilize nude or otherwise immunocompromised mice containing human cancer cells often provide results which are not predictive of results in humans (See Gura, Science, Vol. 278, 11/7/97, pp. 1041-1042).

It must therefore be concluded that the skilled artisan would have had to have conducted undue and excessive experimentation in order to practice the claimed invention.

3. Claims 32, 34, 36-37, 39 and 41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for obtaining expression of a tumor suppressor gene or suicide protein in a cell *in vitro*, does not reasonably provide enablement for said method practiced *in vivo*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rationale underlying the limitation of these claims to the *in vitro* environment is outlined in the above 35 USC 112, 1st paragraph rejection above. The claims are not enabled for the *in vivo* embodiment for the reasons outlined in the above 35 USC 112, 1st paragraph rejection of claims 16-24, 26-31, 33, 35, 38 and 40.

No Claims are allowed.

4. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo whose telephone number is (703) 308-1906. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, George Elliott, can be reached on (703) 308-4003. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242 or (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

David Guzo
April 12, 1999

DAVID GUZO
PRIMARY EXAMINER